

#### **Heart Disease Fact Sheet**

CIRM funds many projects seeking to better understand heart disease and to translate those discoveries into new therapies.

## Description

Heart disease strikes in many forms, but collectively it causes one third of all deaths in the U.S. Many forms of heart disease have a common result—cardiomyopathy. While this is commonly called congestive heart failure (CHF), it is really just the heart becoming less efficient due to any number of causes, but the most common is loss of functioning heart muscle due to the damage caused by a heart attack. An estimated 4.8 million Americans have CHF, with 400,000 new cases diagnosed each year. Half die within five years.

Numerous clinical trials are underway testing a type of stem cell found in bone marrow, called mesenchymal stem cells or MSCs, to see if they are effective in treating the form of CHF that follows a heart attack. While those trials have shown some small improvements in patients the researchers have not found that the MSCs are creating replacement heart muscle. They think the improvements may be due to the MSCs creating new blood vessels that then help make the existing heart muscle healthier, or in other ways strengthening the existing tissue.

California's stem cell agency has numerous awards looking into heart disease (the full list is below). Most of these involve looking for ways to create stem cells that can replace the damaged heart muscle, restoring the heart's ability to efficiently pump blood around the body. Some researchers are looking to go beyond transplanting cells into the heart and are instead exploring the use of tissue engineering technologies, such as building artificial scaffolds in the lab and loading them with stem cells that, when placed in the heart, may stimulate the recovery of the muscle.

Other CIRM-funded researchers are working in the laboratory, looking at stem cells from heart disease patients to better understand the disease and even using those models to discover and test new drugs to see if they are effective in treating heart disease. Other researchers are trying to make a type of specialized heart cell called a pacemaker cell, which helps keep a proper rhythm to the heart's beat.

We also fund projects that are trying to take promising therapies out of the laboratory and closer to being tested in people. In some cases, these awards also fund the early phase clinical trials to show that they are safe to use and, in some cases, show some signs of being effective.

## **Clinical Stage Programs**

## Capricor (Heart failure and Duchenne Muscular Dystrophy-related heart failure)

The company is using donor cells derived from heart stem cells developed by Cedars-Sinai to treat patients developing heart failure after a heart attack. In early studies the cells appear to reduce scar tissue, promote blood vessel growth and improve heart function.

• Read about the team's progress

In a second trial, the company is using the same donor cells derived from heart stem cells to treat patients developing heart failure due to Duchenne Muscular Dystrophy. In early studies the cells appear to reduce scar tissue, promote blood vessel growth and improve heart function.

· Read about the team's progress

## Cedars-Sinai Medical Center (Cardiomyopathy)

This team developed a way to isolate some heart-specific stem cells that are found in adult heart muscle. They use clumps of cells called Cardiospheres to reduce scarring caused by heart attacks. Initially they used cells obtained from the patient's own heart but they later developed methods to obtain the cells they need from donor organs, which allows the procedure to become an off-the-shelf-therapy, meaning it can be available when and where the patient needs it rather than having to create it new each time. The company, working with the Cedars-Sinai team, received FDA approval to begin a clinical trial in June 2012.

• Read about the team's progress

# **Stanford School of Medicine (Heart Failure)**

This team plans to turn embryonic stem cells into what are called cardiomyocytes, the kind of cells that can become heart muscle. They plan to develop methods for producing sufficient quantities for clinical therapy and to do all the laboratory work and preliminary testing needed to gain FDA approval of a clinical trial by the close of the grant. They are proposing to carry out a trial with patients who have disease that is so advanced that they are on a waiting list for heart transplants.

• Read about the team's progress

Video: Bruce Conklin of the Gladstone Institute of Cardiovascular Disease talks about using stem cells to screen drugs for heart side effects

# **CIRM Grants Targeting Heart Disease**

Researcher name	Institution	Grant Title	Grant Type	Approved funds
Walter Boyd	University of California, Davis	Extracellular Matrix Bioscaffold Augmented with Human Stem Cells for Cardiovascular Repair	Early Translational III	\$4,631,754
Christian Metallo	University of California, San Diego	Metabolic regulation of cardiac differentiation and maturation	Basic Biology V	\$1,124,834
Deepak Srivastava	Gladstone Institutes	Direct Cardiac Reprogramming for Regenerative Medicine	Quest - Discovery Stage Research Projects	\$2,400,048
Harold Bernstein	University of California, San Francisco	Modeling Myocardial Therapy with Human Embryonic Stem Cells	Comprehensive Grant	\$2,134,694
Eric Adler	University of California, San Diego	Identification of Novel Therapeutics for Danon Disease Using an iPS Model of the Disease	Early Translational III	\$1,701,575

Eduardo Marbán	Cedars-Sinai Medical Center	[REDACTED] Heart Disease Regenerative Medicine Team Planning Award	Disease Team Planning	\$38,980
Brian Black	University of California, San Francisco	Weinstein Cardiovascular Development Conference	Conference	\$35,000
Robb Maclellan	University of California, Los Angeles	Human Cardiovascular Progenitors, their Niches and Control of Self-renewal and Cell Fate	Basic Biology I	\$917,667
Christopher Zarins	Stanford University	Engineering a Cardiovascular Tissue Graft from Human Embryonic Stem Cells	Comprehensive Grant	\$2,454,490
Yang Xu	University of California, San Diego	Human ES cell based therapy of heart failure without allogenic immune rejection	Early Translational III	\$1,857,600
Mark Mercola	Sanford- Burnham Medical Research Institute	"Stem Cell Therapies for Heart Failure"	Disease Team Planning	\$44.450
Alice Tarantal	University of California, Davis	11th Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases	Conference	\$16,850
Eduardo Marbán	Cedars-Sinai Medical Center	Autologous cardiac-derived cells for advanced ischemic cardiomyopathy	Disease Team Research I	\$5,560,232
Deepak Srivastava	Gladstone Institutes	microRNA Regulation of Cardiomyocyte Differentiation from Human Embryonic Stem Cells	Comprehensive Grant	\$2,994,719
Rachel Smith	Capricor, Inc	Allogeneic Cardiac-Derived Stem Cells for Patients Following a Myocardial Infarction	Disease Team Therapy Development - Research	\$14,405,857
Michelle Khine	University of California, Merced	Micro Platform for Controlled Cardiac Myocyte Differentiation	SEED Grant	\$193,700
Alice Tarantal	University of California, Davis	gth Annual Gene Therapy Symposium for Heart, Lung and Blood Diseases	Conference	\$12,000
Bruce Conklin	Gladstone Institutes	Induced Pluripotent Stem Cells for Cardiovascular Diagnostics	New Cell Lines	\$1,708,560
Mark Mercola	Sanford- Burnham Medical Research Institute	Chemical Genetic Approach to Production of hESC-derived Cardiomyocytes	Comprehensive Grant	\$2,832,000

Joseph Wu	Stanford University	Human Embryonic Stem Cell-Derived Cardiomyocytes for Patients with End Stage Heart Failure	Disease Team Therapy Development - Research	\$19,060,330
Todd McDevitt	Gladstone Institutes	Engineering microscale tissue constructs from human pluripotent stem cells	Research Leadership	\$5,884,058
Alice Tarantal	University of California, Davis	10th Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases	Conference	\$18,300
Michael Longaker	Stanford University	Derivation and analysis of pluripotent stem cell lines with inherited TGF-b mediated disorders from donated IVF embryos and reprogrammed adult skin fibroblasts	New Cell Lines	\$1,406,636
Patrick McDonough	Vala Sciences, Inc.	Optimization in the Identification, Selection and Induction of Maturation of Subtypes of Cardiomyocytes derived from Human Embryonic Stem Cells	Tools and Technologies I	\$870,717
Huei-sheng Chen	Sanford- Burnham Medical Research Institute	Studying Arrhythmogenic Right Ventricular Dysplasia with patient-specific iPS cells	Basic Biology IV	\$1,579,250
Michael Snyder	Stanford University	Center of Excellence for Stem Cell Genomics - Stanford	Genomics Centers of Excellence Awards (R)	\$22,796,609
Joseph Wu	Stanford University	A Novel, Robust and Comprehensive Predictive Tool Using Human Disease-Specific Induced Pluripotent Stem Cells for Preclinical Drug Screening	Tool Translational Research Projects	\$1,000,000
Sylvia Evans	University of California, San Diego	Specification of Ventricular Myocyte and Pacemaker Lineages Utilizing Human Embryonic Stem Cells	SEED Grant	\$585,600
Mohammad Pashmforoush	University of Southern California	Transcriptional Regulation of Cardiac Pacemaker Cell Progenitors	New Faculty I	\$2,816,578
Benoit Bruneau	Gladstone Institutes	Epigenetic regulation of human cardiac differentiation	Basic Biology IV	\$1,568,148
Joseph Gold	City of Hope	Development of a scalable, practical, and transferable GMP-compliant suspension culture-based differentiation process for cardiomyocyte production from human embryonic stem cells.	Tools and Technologies III	\$891,518
Sonja Schrepfer	University of California, San Francisco	Hypo-immunogenic cardiac patches for myocardial regeneration	Inception - Discovery Stage Research Projects	\$238,500
Krishna Shenoy	Stanford University	Technology for hESC-Derived Cardiomyocyte Differentiation and Optimization of Graft-Host Integration in Adult Myocardium	SEED Grant	\$572,891

Deborah Lieu California. Davis Induction of Pluripotent Stem Cell-Derived Pacemaking Celts California. Davis California. Davis California. San Diego California. Service Engineering Tissue Engineering Celts Derived Cardiomyccytes for Cardiac Tachenologies III Sala8.517 Colora California. Berketely California. Berketely California. Discovering Potent Molecules with Human ESCs to Treat Research Research Research Institute California Califo	Andrew Putnam	University of California, Irvine	A Novel Engineered Niche to Explore the Vasculogenic Potential of Embryonic Stem Cells	New Faculty I	\$395,764	
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Deborah Lieu California, Davis Stage Research Projects \$2,042,728	Joseph Wu			Conference II	\$7.500	
Michelle University of Nt. Plute of Colonial Difference Colonial D	Deborah Lieu	California,		Stage Research	\$2,042,728	
Khine California, Irvine Califor			Micro Platform for Controlled Cardiac Myocyte Differentiation	SEED Grant	\$156,426	

Farah Sheikh	University of California, San	Molecular Mechanisms Underlying Human Cardiac Cell	Basic Biology III	\$1,341,955
	Diego	Junction Maturation and Disease Using Human iPSC		
Ali Nsair	University of California, Los Angeles	Human Induced Pluripotent Stem Cell-Derived Cardiovascular Progenitor Cells for Cardiac Cell Therapy.	New Faculty Physician Scientist	\$2,316,894
Linda Cambier	Cedars-Sinai Medical Center	Exosomal Y-RNAs as mediators of bioactivity of cardiac- derived cell therapy	Inception - Discovery Stage Research Projects	\$181,063
Jane Lebkowski	Geron Corporation	Preclinical Development and First-In-Human Testing of GRNCM1 in Advanced Heart Failure	Disease Team Therapy Planning	\$0
Phillip Yang	Stanford University	In Vivo Molecular Magnetic Resonance Imaging of Human Embryonic Stem Cells in Murine Model of Myocardial Infarction	SEED Grant	\$629,952
Sean Wu	Stanford University	Elucidating Molecular Basis of Hypertrophic Cardiomyopathy with Human Induced Pluripotent Stem Cells	Basic Biology III	\$1,260,537
Reza Ardehali	University of California, Los Angeles	Preclinical evaluation of human embryonic stem cell-derived cardiovascular progenitors in a large animal model	New Faculty Physician Scientist	\$2,930,388
Phillip Yang	Stanford University	Activation of patient-specific endogenous myocardial repair through the exosomes generated from the hypoxic iPSC-derived cardiomyocytes (iCMs).	Inception - Discovery Stage Research Projects	\$234,619
Benoit Bruneau	Gladstone Institutes	Induction of cardiogenesis in pluripotent cells via chromatin remodeling factors	New Faculty II	\$2,723,653
John Laird	University of California, Davis	Phase I study of IM Injection of VEGF Producing MSC for the Treatment of Critical Limb Ischemia	Disease Team Therapy Planning	\$76,066
Joseph Wu	Stanford University	Tissue Collection for Accelerating iPSC Research in Cardiovascular Diseases	Tissue Collection for Disease Modeling	\$1,291,832
Arjun Deb	University of California, Los Angeles	Targeting progenitors in scar tissue to reduce chronic scar burden	Inception - Discovery Stage Research Projects	\$230,400
Ching-Pin Chang	Stanford University	VEGF signaling in adventitial stem cells in vascular physiology and disease	New Faculty II	\$3,005,695
Robert Robbins	Stanford University	Human Embryonic Stem Cell-Derived Cardiomyocytes for Patients with End Stage Heart Failure	Disease Team Therapy Planning	\$73,030

Thomas Novak	Cellular Dynamics International	Generation and characterization of high-quality, footprint-free human induced pluripotent stem cell lines from 3,000 donors to investigate multigenic diseases	hiPSC Derivation	\$16,000,000
Deepak Srivastava	Gladstone Institutes	Use of Human iPSC-derived Endothelial Cells for Calcific Aortic Valve Disease Therapeutics	Quest - Discovery Stage Research Projects	\$2,400,048
Kara McCloskey	University of California, Merced	Building Cardiac Tissue from Stem Cells and Natural Matrices	New Faculty II	\$1,656,083
Deepak Srivastava	Gladstone Institutes	Direct Cardiac Reprogramming for Heart Regeneration	Early Translational III	\$5,795,871
Deborah Requesens	Coriell Institute for Medical Research	The CIRM Human Pluripotent Stem Cell Biorepository – A Resource for Safe Storage and Distribution of High Quality iPSCs	hPSC Repository	\$9,942,175
Deborah Ascheim	Capricor, Inc	Allogeneic Cardiosphere-Derived Cells for Duchenne Muscular Dystrophy Cardiomyopathy	Clinical Trial Stage Projects	\$3,376,259
Irving Weissman	Stanford University	Prospective isolation of hESC-derived hematopoietic and cardiomyocyte stem cells	Comprehensive Grant	\$2,471,386
Joseph Wu	Stanford University	Heart Repair with Human Tissue Engineered Myocardium	Early Translational III	\$4,396,738
John Cashman	Human BioMolecular Research Institute	Improving Existing Drugs for Long QT Syndrome type 3 (LQT3) by hiPSC Disease-in-Dish Model	Early Translational IV	\$6,361,369
Michael Lewis	Cedars-Sinai Medical Center	Pulmonary Arterial Hypertension Treated with Cardiosphere- Derived Allogeneic Stem Cells	Clinical Trial Stage Projects	\$7,354,772
Randall Lee	University of California, San Francisco	Embryonic Stem Cell-Derived Therapies Targeting Cardiac Ischemic Disease	Comprehensive Grant	\$2,424,353

# **CIRM Heart Disease Videos**



Growing Stem Cell Research in California: Todd McDevitt Lab, Gladstone Institutes



Heart disease: Progress toward stem cell therapies, a live Google Hangout



Webinar: Stem Cell Clinical Trial for Heart Disease - Lessons Learned | Eduardo Marbán



Yen Bui, Gladstone Institutes -CIRM Stem Cell #SciencePitch



Deepak Srivastava, Gladstone Institutes - CIRM Stem Cell #SciencePitch



Spotlight on Stem Cell Advances in Pediatric Heart Disease: A Change of Heart



Spotlight on Stem Cell Advances in Heart Disease: Generating Muscle within an Existing Heart



Joshua's Heart Story: Pediatric Heart Disease and the Promise of Stem Cell Advances



Stem Cell Clinical Trial for Heart Failure: Eduardo Marbán - CIRM Spotlight on Disease



Cardiovascular Therapies: Spotlight on Stem Cell Research - Welcoming Remarks



Cardiovascular Therapies: Spotlight on Stem Cell Research - W. Douglas Boyd



Cardiovascular Therapies: Spotlight on Stem Cell Research - Yung-Wei Chi



Cardiovascular Therapies: Spotlight on Stem Cell Research - Jeanette Owens



Valentine's Day Stem Cell Wish: Mending Broken Hearts



Stem Cell-Derived Heart Cells: Bruce Conklin - CIRM Science Writer's Seminar

#### Resources

- Blogs on heart disease research from the CIRM Stem Cellar
- NIH: Heart Failure Information
- Find a clinical trial near you: NIH Clinical Trials database
- American Heart Association
- National Heart, Lung and Blood Institute
- CDC: Heart Disease

## Find Out More:

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